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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,634	06/20/2003	Kevin Gunderson	01-00003	7176

29389 7590 11/27/2006

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EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,634	GUNDERSON ET AL.	
	Examiner	Art Unit	
	Angela Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-26,28-34,36-51,53,54,64,66-72 and 78-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17-26,28-34,36-51,53,54,64,66-72 and 78-80* is/are rejected.

7)☒ Claim(s) *9 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/26/06, 7/13/06, 7/14/06, 7/24/06.

FINAL REJECTION

Status of the Application

1. Applicant's response filed June 16, 2006 is acknowledged. Claims 1-15, 17-26, 28-34, 36-51, 53, 54, 64, 66-72, and 78-80 are currently pending. Claims 78-80 are new.

Claim Objections

2. Claim 9 is objected to because of the following informalities: This claim depends from a cancelled claim, claim 8. Appropriate correction is required.

Claim 36 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 36 depends from claim 18. Claim 18 recites in step (c) "directly detecting typable loci of probe-fragment hybrids". Claim 36 recites "the method of claim 18, wherein step (c) comprises directly detecting typable loci of fragments that hybridize to the probes." Since claim 36 simply reiterates the limitation already present in step (c) of claim 18, it fails to further limit claim 18 from which it depends.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 3-7, 9-12, 14, 15, 17-19, 22-26, 28-31, 33, 34, 36, 37, 39-48, 50, and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Schubert et al. (American Journal of Pathology (January 2002) 160(1): 73-79; newly cited) as evidenced by the following: Lindblad-Toh et al. (Nature Biotechnology (2000) 18: 1001-1005; newly cited), Zhang et al. (PNAS (1992) 89: 5847-5851; cited previously), and Roche technical information (cited previously).

Regarding claim 1, Schubert teaches a method of detecting typable loci of a genome, comprising:

(a) amplifying genomic DNA with a population of random primers, thereby providing an amplified representative population of genome fragments comprising said typable loci, wherein said population comprises a high complexity representation (page 74, column 2 teaches whole genome amplification of genomic DNA by PEP according to the method taught by Zhang. Zhang teaches on page 5847 that PEP is conducted using random primers and generates a high complexity representation)

(b) contacting said genome fragments with a plurality of immobilized nucleic acid probes having sequences corresponding to said typable loci under conditions wherein probe-fragment hybrids are formed, wherein said probes are at most 125 nucleotides in length (page 75, column 1 teaches that gDNA subjected to PEP was hybridized to the HuSNP array as described by Lindblad-Toh. Lindblad-Toh teaches on page 1001 that the HuSNP array contains 25–mer probes for 1494 loci)

(c) detecting typable loci of said probe-fragment hybrids (page 77).

Regarding claim 3, Schubert teaches that the providing in step (a) comprises representationally amplifying a native genome (page 74, column 2, where the PEP whole genome amplification procedure is a representational amplification)

Regarding claim 4, Schubert teaches that the representationally amplifying comprises using a polymerase of low processivity (page 74, column 2 teaches that whole genome amplification was performed as taught by Zhang. Zhang teaches on page 5847, column 2, that Taq polymerase is used at 55°C).

Regarding claim 5, the Taq polymerase used by Schubert inherently has a processivity rate of less than 100 bases per polymerization event (see Roche PCR applications manual, Chapter 2, where Taq polymerase is shown to have a processivity of 50 bp at the above reaction temperature).

Regarding claim 6, Schubert teaches that the representationally amplifying comprises a single step reaction yielding a high complexity representation (page 74, column 2 teaches that whole genome amplification was preformed as taught by Zhang. Zhang teaches on page 5847, that the PEP reaction comprises a single step reaction). A "single step reaction" has been interpreted to mean a "closed tube" reaction, because according to the specification, the term "a single step reaction" only appears to differentiate between the pooling of multiple, separate amplifications and performing a single amplification reaction (paragraph 153). Also, in the Examples, only single amplification reactions comprising multiple different temperature steps were conducted to produce representationally amplified samples. Therefore, the disclosure of Schubert as evidenced by Zhang meets the instant limitation.

Regarding claim 7, Schubert teaches that at most 1 x 10^6 copies of said native genome are used as a template for amplification (page 74, column 2, where the 7 ng of gDNA used by Schubert in the PEP reaction comprises approximately 350 copies of the native genome).

Regarding claim 9, Schubert teaches that the substrate is a surface (page 75, column 1, where the HuSNP array was used).

Regarding claim 10, Schubert teaches that at least 100 typable loci are simultaneously detected (see Figure 1 and Tables 3 and 4).

Regarding claim 11, Schubert teaches that the genome is a human genome (page 74).

Regarding claim 12, Schubert teaches that step (b) of claim 1 comprises contacting the genome fragments with a multiplexed array of nucleic acid probes (page 74, column 2 – page 75, column 1).

Regarding claim 14, Schubert teaches that the probes are nucleic acid probes that are at least 20 nucleotides in length (Schubert teaches hybridization of the genome fragments to the HuSNP array on page 75, column 1 as described by Lindblad-Toh. Lindblad-Toh teaches on page 1001 that this array consists of 25-mer probes for typing 1494 loci).

Regarding claim 15, Schubert teaches producing a report identifying said typable loci that are detected (the published is a report identifying the typable loci that were detected – see Figure 1 and Tables 3 & 4).

Regarding claim 17, Schubert teaches that step (c) of claim 1 comprises directly detecting said typable loci of said fragments that hybridize to said probes (page 75, column 1, where the HuSNP array is used to directly detect typable loci. See pages 1003-1004 of the cited reference Lindblad-Toh for further description of array hybridization and analysis).

Regarding claim 18, Schubert teaches a method of detecting typable loci of a genome, comprising:

(a) amplifying genomic DNA with a population of random primers, thereby providing an amplified representative population of genome fragments comprising said typable loci (page 74, column 2 teaches whole genome amplification of genomic DNA by PEP according to the method taught by Zhang. Zhang teaches on page 5847 that PEP is conducted using random primers)

(b) contacting said genome fragments with a plurality of immobilized nucleic acid probes having sequences corresponding to said typable loci under conditions wherein probe-fragment hybrids are formed (page 75, column 1 teaches that gDNA subjected to PEP was hybridized to the HuSNP array as described by Lindblad-Toh. Lindblad-Toh teaches on page 1001 that the HuSNP array contains 25–mer probes for 1494 loci)

(c) directly detecting typable loci of said probe-fragment hybrids (page 77; See pages 1003-1004 of the cited reference Lindblad-Toh for further description of array hybridization and analysis).

Regarding claim 19, Schubert teaches that about 350 copies of the native genome are amplified (page 74, column 2, where the 7 ng of gDNA used by Schubert in the PEP reaction comprises approximately 350 copies of the native genome).

Regarding claim 22, Schubert teaches that the providing in step (a) comprises representationally amplifying a native genome (page 74, column 2, where the PEP whole genome amplification procedure is a representational amplification).

Regarding claim 23, Schubert teaches that the representatiorially amplifying comprises using a polymerase of low processivity (page 74, column 2 teaches that whole genome

amplification was performed as taught by Zhang. Zhang teaches on page 5847, column 2, that Taq polymerase is used at 55°C).

Regarding claim 24, Schubert teaches that the low processivity is less than 100 bases per polymerization event (see Roche PCR applications manual, Chapter 2, where Taq polymerase is shown to have a processivity of 50 bp at the above reaction temperature).

Regarding claim 25, Schubert teaches disclose the method of claim 22, wherein said representationally amplifying comprises a single step reaction yielding a high complexity representation (page 74, column 2 teaches that whole genome amplification was preformed as taught by Zhang. Zhang teaches on page 5847, that the PEP reaction comprises a single step reaction).

Regarding claim 26, Schubert teaches that at most 1×10^6 copies of the native genome are used as a template for amplification (page 74, column 2, where the 7 ng of gDNA used as a template correspond to approximately 350 copies of the native genome).

Regarding claim 28, Schubert teaches that the substrate is a surface (page 75, column 1, where the HuSNP array was used).

Regarding claim 29, Schubert teaches that at least 100 typable loci are simultaneously detected (see Figure 1 and Tables 3 and 4).

Regarding claim 30, Schubert teaches the method of claim 18, wherein said genome is a human genome (page 74).

Regarding claim 31, Schubert teaches that step (b) of claim 18 comprises contacting the genome fragments with a multiplexed array of nucleic acid probes (page 74, column 2 – page 75, column 1).

Regarding claim 33, Schubert teaches that the probes are nucleic acid probes that are at least 20 nucleotides in length (Schubert teaches hybridization of the genome fragments to the HuSNP array on page 75, column 1 as described by Lindblad-Toh. Lindblad-Toh teaches on page 1001 that this array consists of 25-mer probes for typing 1494 loci).

Regarding claim 34, Schubert teaches the method of claim 18, further comprising producing a report identifying said typable loci that are detected (the published is a report identifying the typable loci that were detected – see Figure 1 and Tables 3 & 4).

Regarding claim 36, Schubert teaches the method of claim 18, wherein step (c) comprises directly detecting said typable loci of said fragments that hybridize to said probes (page 75, column 1, where the HuSNP array is used to directly detect typable loci. See pages 1003-1004 of the cited reference Lindblad-Toh for further description of array hybridization and analysis).

Regarding claim 37, Schubert teaches a method of detecting typable loci of a genome, comprising the steps of:

(a) amplifying genomic DNA with a population of random primers, thereby providing an amplified representative population of genome fragments comprising said typable loci, wherein the population of amplified genomic fragments comprises a high complexity representation (page 74, column 2 teaches whole genome amplification of genomic DNA by PEP according to the method taught by Zhang. Zhang teaches on page 5847 that PEP is conducted using random primers and generates a high complexity representation)

(b) contacting said genome fragments with a plurality of immobilized nucleic acid probes having sequences corresponding to said typable loci under conditions wherein immobilized probe-fragment hybrids are formed (page 75, column 1 teaches that gDNA subjected to PEP was

hybridized to the HuSNP array as described by Lindblad-Toh. Lindblad-Toh teaches on page 1001 that the HuSNP array contains 25–mer probes for 1494 loci)

(c) modifying said immobilized probe-fragment hybrids (page 75, column 1 teaches hybridization to the HuSNP array as described by Lindblad-Toh. Lindblad-Toh teaches on page 1004 that the probe-fragment hybrids were treated (or modified) by staining with streptavidin-phycoerythrin and biotinylated antistreptavidin antibody)

(d) detecting a probe or fragment modified in step (c), thereby detecting said typable loci of said genome (page 77; See pages 1003-1004 of the cited reference Lindblad-Toh for further description of array hybridization and analysis).

Regarding claim 39, Schubert teaches that the providing in step (a) comprises representationally amplifying a native genome (page 74, column 2, where the PEP whole genome amplification procedure is a representational amplification).

Regarding claim 40, Schubert teaches that the representatiorially amplifying comprises using a polymerase of low processivity (page 74, column 2 teaches that whole genome amplification was performed as taught by Zhang. Zhang teaches on page 5847, column 2, that Taq polymerase is used at 55°C).

Regarding claim 41, Schubert teaches that the low processivity is less than 100 bases per polymerization event (see Roche PCR applications manual, Chapter 2, where Taq polymerase is shown to have a processivity of 50 bp at the above reaction temperature).

Regarding claim 42, Schubert teaches that said representationally amplifying comprises a single-step reaction yielding a high complexity representation (page 74, column 2 teaches that

whole genome amplification was preformed as taught by Zhang. Zhang teaches on page 5847, that the PEP reaction comprises a single step reaction).

Regarding claim 43, Schubert teaches that at most 1 x 10^6 copies of said native genome are used as a template for amplification (page 74, where the 7 ng of gDNA used by Schubert in the PEP reaction corresponds to approximately 350 copies of the native genome).

Regarding claim 44, Schubert teaches that the nucleic acid probes are immobilized on a substrate (page 75, column 1, where the HuSNP array is an array of substrate-immobilized nucleic acid probes).

Regarding claim 45, Schubert teaches that the substrate is selected from the group consisting of a particle, bead, surface, slide, and microchip (page 75, column 1, where the HuSNP array is a surface comprising immobilized nucleic acid probes).

Regarding claim 46, Schubert teaches that least 100 typable loci are simultaneously detected (see Figure 1 and Tables 3 and 4).

Regarding claim 47, Schubert teaches disclose the method of claim 37, wherein said genome is a human genome (page 74).

Regarding claim 48, Schubert teaches the method of claim 37, wherein step (b) comprises contacting said genome fragments with a multiplexed array of nucleic acid probes (page 74, column 2 – page 75, column 1).

Regarding claim 50, Schubert teaches that the probes comprise nucleic acid probes that are at least 20 nucleotides in length (Schubert teaches hybridization of the genome fragments to the HuSNP array on page 75, column 1 as described by Lindblad-Toh. Lindblad-Toh teaches on page 1001 that this array consists of 25-mer probes for typing 1494 loci).

Regarding claim 51, Schubert teaches the method of claim 37, further comprising producing a report identifying said typable loci that are detected (the published is a report identifying the typable loci that were detected – see Figure 1 and Tables 3 & 4).

5. Claims 1-3, 6, 7, 9-12, 14, 15, 17-20, 22, 25, 26, 28-31, 33, 34, 36, 37, 39, 42-48, 50, 51, 64, 72, and 78-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al. (US 6,617,137 B2; cited on IDS). This patent obtains benefit of US Application 09/977,868, filed October 15, 2001.

Regarding claim 1, Dean teaches a method of detecting typable loci of a genome, comprising:

(a) amplifying genomic DNA with a population of random primers, thereby providing an amplified representative population of genome fragments comprising said typable loci, wherein said population comprises a high complexity representation (column 37, lines 10-39)

(b) contacting said genome fragments with a plurality of immobilized nucleic acid probes having sequences corresponding to said typable loci under conditions wherein probe-fragment hybrids are formed, wherein said probes are at most 125 nucleotides in length (column 16, lines 26-50 teaches address probes less than 125 nucleotides in length; column 18, lines 39-41 teach hybridization of amplification products to these surface-immobilized probes)

(c) detecting typable loci of said probe-fragment hybrids (column 16, lines 26-50 and column 18, lines 39-54).

Regarding claim 2, Dean teaches that the population of representative genome fragments comprises sequences identical to at least 90% of the genome (see Figure 6 and column 40, lines 51-61).

Regarding claim 3, Dean teaches that the providing in step (a) comprises representationally amplifying a native genome (the amplification conducted in column 37, lines 10-39 is a representational amplification).

Regarding claim 6, Dean teaches the representational amplification is a single-step reaction yielding a high complexity representation (column 37, lines 10-39 teach a single-step procedure). As noted above, a "single step reaction" has been interpreted to mean a "closed tube" reaction, because according to the specification, the term "a single step reaction" only appears to differentiate between the pooling of multiple, separate amplifications and performing a single amplification reaction (paragraph 153). Also, in the Examples, only single amplification reactions comprising multiple different temperature steps were conducted to produce representationally amplified samples. Therefore, the disclosure of Dean meets the instant limitation.

Regarding claim 7, Dean teaches that at most 1×10^6 copies of said native genome are used as a template for amplification (column 39, lines 31-33, where 9 copies were used).

Regarding claim 9, Dean teaches that the substrate is a particle, a bead, a surface, a slide or a microchip (column 18, lines 23-38).

Regarding claim 10, Dean teaches that at least 100 typable loci are simultaneously detected (column 19, lines 51-52 teaches detection of 256 targets).

Regarding claim 11, Dean teaches that the genome is a human genome (column 37, lines 10-12).

Regarding claim 12, Dean teaches that step (b) of claim 1 comprises contacting the genome fragments with a multiplexed array of nucleic acid probes (column 18, lines 39-41).

Regarding claim 14, Dean teaches that the probes are nucleic acid probes that are at least 20 nucleotides in length (column 16, lines 26-50 teaches that the address probes described in column 18, lines 39-41 are less than 125 nucleotides in length, specifically 15-20 nucleotides in length).

Regarding claim 15, Dean teaches producing a report identifying said typable loci that are detected (column 17, lines 25-28).

Regarding claim 17, Dean teaches that step (c) of claim 1 comprises directly detecting said typable loci of said fragments that hybridize to said probes (column 18, lines 39-41 teach hybridization of the amplified products to an oligonucleotide microarray; column 20, lines 7-20 teach coupling a detectable label to the detection (i.e. address) probes).

Regarding claim 18, Dean teaches a method of detecting typable loci of a genome, comprising:

(a) amplifying genomic DNA with a population of random primers, thereby providing an amplified representative population of genome fragments comprising said typable loci (column 37, lines 10-39)

(b) contacting said genome fragments with a plurality of immobilized nucleic acid probes having sequences corresponding to said typable loci under conditions wherein probe-fragment hybrids are formed (column 16, lines 26-50 teaches address probes less than 125 nucleotides in

length; column 18, lines 39-41 teach hybridization of amplification products to these surface-immobilized probes)

(c) directly detecting typable loci of said probe-fragment hybrids (column 18, lines 39-41 teach hybridization of the amplified products to an oligonucleotide microarray; column 20, lines 7-20 teach coupling a detectable label to the detection (i.e. address) probes).

Regarding claim 19, Dean teaches that 9 copies of the native genome are amplified (column 39, lines 31-33).

Regarding claim 20, Dean teaches that the population of representative genome fragments comprises sequences identical to at least 90% of the genome (see Figure 6 and column 40, lines 51-61).

Regarding claim 22, Dean teaches that the providing in step (a) comprises representationally amplifying a native genome (the amplification conducted in column 37, lines 10-39 is a representational amplification).

Regarding claim 25, Dean teaches disclose the method of claim 22, wherein said representationally amplifying comprises a single step reaction yielding a high complexity representation (column 37, lines 10-39 teach a single-step procedure).

Regarding claim 26, Dean teaches that at most 1×10^6 copies of the native genome are used as a template for amplification (column 39, lines 31-33, where 9 copies were used).

Regarding claim 28, Dean teaches that the substrate is a particle, a bead, a surface, a slide or a microchip (column 18, lines 23-38).

Regarding claim 29, Dean teaches that at least 100 typable loci are simultaneously detected (column 19, lines 51-52 teaches detection of 256 targets).

Regarding claim 30, Dean teaches the method of claim 18, wherein said genome is a human genome (column 37, lines 10-12).

Regarding claim 31, Dean teaches that step (b) of claim 18 comprises contacting the genome fragments with a multiplexed array of nucleic acid probes (column 18, lines 39-41).

Regarding claim 33, Dean teaches that the probes are nucleic acid probes that are at least 20 nucleotides in length (column 16, lines 26-50 teaches that the address probes described in column 18, lines 39-41 are less than 125 nucleotides in length, specifically 15-20 nucleotides in length).

Regarding claim 34, Dean teaches the method of claim 18, further comprising producing a report identifying said typable loci that are detected (column 17, lines 25-28).

Regarding claim 36, Dean teaches the method of claim 18, wherein step (c) comprises directly detecting said typable loci of said fragments that hybridize to said probes (column 18, lines 39-41 teach hybridization of the amplified products to an oligonucleotide microarray; column 20, lines 7-20 teach coupling a detectable label to the detection (i.e. address) probes).

Regarding claim 37, Dean teaches a method of detecting typable loci of a genome, comprising the steps of:

(a) amplifying genomic DNA with a population of random primers, thereby providing an amplified representative population of genome fragments comprising said typable loci, wherein the population of amplified genomic fragments comprises a high complexity representation (column 37, lines 10-39)

(b) contacting said genome fragments with a plurality of immobilized nucleic acid probes having sequences corresponding to said typable loci under conditions wherein immobilized

probe-fragment hybrids are formed (column 16, lines 26-50 teaches address probes less than 125 nucleotides in length; column 18, lines 39-41 teach hybridization of amplification products to these surface-immobilized probes)

(c) modifying said immobilized probe-fragment hybrids (column 34, line 60 – column 35, line 10 teach modification of the immobilized probe-fragment hybrids by contacting biotin-labeled immobilized nucleic acids with alkaline phosphatase-streptavidin conjugate)

(d) detecting a probe or fragment modified in step (c), thereby detecting said typable loci of said genome (column 34, line 60 – column 35, line 10).

Regarding claim 39, Dean teaches that the providing in step (a) comprises representationally amplifying a native genome (the amplification conducted in column 37, lines 10-39 is a representational amplification).

Regarding claim 42, Dean teaches that said representationally amplifying comprises a single-step reaction yielding a high complexity representation (column 37, lines 10-39 teach a single-step procedure).

Regarding claim 43, Dean teaches that at most 1×10^6 copies of said native genome are used as a template for amplification (column 39, lines 31-33, where 9 copies were used).

Regarding claims 44 and 45, Dean teaches that the nucleic acid probes are immobilized on a substrate, specifically a particle, a bead, a surface, a slide or a microchip (column 18, lines 23-38).

Regarding claim 46, Dean teaches that least 100 typable loci are simultaneously detected (column 19, lines 51-52 teaches detection of 256 targets).

Regarding claim 47, Dean teaches disclose the method of claim 37, wherein said genome is a human genome (column 37, lines 10-12).

Regarding claim 48, Dean teaches the method of claim 37, wherein step (b) comprises contacting said genome fragments with a multiplexed array of nucleic acid probes (column 18, lines 39-41).

Regarding claim 50, Dean teaches that the probes comprise nucleic acid probes that are at least 20 nucleotides in length (column 16, lines 26-50 teaches that the address probes described in column 18, lines 39-41 are less than 125 nucleotides in length, specifically 15-20 nucleotides in length).

Regarding claim 51, Dean teaches the method of claim 37, further comprising producing a report identifying said typable loci that are detected (column 17, lines 25-28).

Regarding claim 64, Dean teaches a method for detecting typable loci of a genome, comprising the steps of:

(a) in vitro transcribing a population of amplified genome fragments, thereby obtaining genomic RNA fragments, wherein the population of amplified genomic fragments is produced by amplification with a plurality of random primers to produce a high complexity representation (column 35, lines 42)

(b) hybridizing said genomic RNA fragments with a plurality of nucleic acid probes having sequences corresponding to said typable loci, thereby forming a plurality of RNA fragment-probe hybrids (column 18, lines 39-41 teach hybridization of amplification products to these surface-immobilized probes)

(c) detecting typable loci of said RNA fragment-probe hybrids (column 18, lines 39-41)

Regarding claim 72, Dean teaches that the method of claim 64 further comprises a step of isolating said genomic RNA fragments (column 18, lines 35-51).

Regarding claims 78-80, Dean teaches that in the method of claims 1, 18, and 37, the genomic DNA is amplified under isothermal conditions using a polymerase with strand displacement activity (see column 37, lines 36-37, where phi 29 DNA polymerase is used; see also column 24, lines 24-57).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 13, 32, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Schubert et al. (American Journal of Pathology (January 2002) 160(1): 73-79; newly cited) as evidenced by the following: Lindblad-Toh et al. (Nature Biotechnology (2000) 18: 1001-1005; newly cited), Zhang et al. (PNAS (1992) 89: 5847-5851; cited previously), and Roche technical information (cited previously) **or** Dean et al. (US 6,617,137 B2) in view of Maldonago-Rodriguez (Molecular Biotechnology, 1999; cited previously).

Schubert as evidenced by the following: Lindblad-Toh, Zhang, and Roche technical information teaches the method of claims 1, 18, and 37, as discussed above. Likewise, Dean teaches the method of claims 1, 18, and 37, as discussed above.

These references do not teach contacting the array of nucleic acid probes with chaperone probes.

Maldonado-Rodriguez taught that preannealing auxiliary oligonucleotides to targets prior to contacting them with immobilized probes resulted in substantial increases in hybridization specificity and sensitivity as well as signal amplification (see abstract, especially points (1) – (4)). These auxiliary oligonucleotides are the functional equivalent of the instantly claimed chaperone probes.

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize chaperone probes (or analogously "auxiliary oligonucleotides") as taught by Maldonado-Rodriguez in the method taught by either Schubert **or** Dean in order to improve hybridization specificity, sensitivity and amplify the observed signal. Maldonado-Rodriguez particularly pointed out that the preannealing of these chaperone probes to target sequences prior to hybridization to array-immobilized probes resulted in improved mismatch detection,

amplification of the observed signal via base-stacking interactions between the chaperone probe and target sequence, and increased sensitivity by prevention of hybridization-blocking secondary structure formation in the target (see abstract and Discussion). These improvements to array-based hybridization experiments would have been directly applicable to the ordinary practitioner of the method taught by Schubert **or** Dean and would have strongly motivated this ordinary artisan to utilize chaperone probes as taught by Maldonado-Rodriguez in order to improve the hybridization-based analysis method in the ways outlined above.

8. Claims 21 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dean et al. (US 6,617,137 B2) in view of Lipshutz et al. (Nature Genetics (1999) 21: 20-24; newly cited).

Dean teaches the method of claims 18 and 37, as discussed above.

Dean teaches hybridization to high-density oligonucleotide arrays, but does not comment specifically as to how many different probes are present on the arrays.

Lipshutz teaches production and applications of high-density oligonucleotide arrays (see abstract). Regarding claims 21 and 38, Lipshutz teaches oligonucleotide arrays with 7,000 – 40,000 genes/ESTs per array (see Table 1 and Table 2), corresponding to greater than 10% of expressed human genes. Lipshutz teaches that these arrays are capable of quantitative and highly parallel expression monitoring (see abstract).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize a high-density oligonucleotide array as taught by Lipshutz to quantify amplification products generated by the method of Dean. Lipshutz expressly taught that the above high-density oligonucleotide arrays afforded the ability to simultaneously quantify more

than 7,000 different genes (see Table 1). Since Dean taught that the multiple displacement amplification method described above was applicable to expression profiling (column 16, lines 51-67), an ordinary practitioner of this embodiment would have been motivated by the teachings of Lipshutz to monitor the expression profile using high-density oligonucleotide arrays, in order to obtain a rapid, quantitative, high-throughput method of monitoring the expression of a number of different genes. An ordinary practitioner would have expected a reasonable level of success in hybridizing the MDA products generated by the method of Dean to high-density oligonucleotide arrays, since Dean expressly taught hybridization to such arrays (column 18, lines 39-41). Therefore, one of ordinary skill in the art, interested in obtaining a rapid quantitative, high-throughput method of analyzing the amplified products generated by the method of Dean, would have been motivated to utilize the high-density oligonucleotide arrays taught by Lipshutz, thus resulting in the instantly claimed methods.

9. Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Schubert et al. (American Journal of Pathology (January 2002) 160(1): 73-79; newly cited) as evidenced by the following: Lindblad-Toh et al. (Nature Biotechnology (2000) 18: 1001-1005; newly cited), Zhang et al. (PNAS (1992) 89: 5847-5851; cited previously), and Roche technical information (cited previously) **or** Dean et al. (US 6,617,137 B2) in view of Pastinen et al. (Genome Research (1997) 7: 606-614; newly cited).

Schubert et al. (American Journal of Pathology (January 2002) 160(1): 73-79; newly cited) as evidenced by the following: Lindblad-Toh et al. (Nature Biotechnology (2000) 18:

1001-1005; newly cited), Zhang et al. (PNAS (1992) 89: 5847-5851; cited previously), and Roche technical information (cited previously) teach the method of claim 37, as discussed above.

Likewise, Dean teaches the method of claim 37, as discussed above.

These references teach genotyping based on array hybridization rather than solid-phase primer extension.

Pastinen teaches a method for multiplexed mutation analysis comprising: (a) multiplex PCR amplification, (b) hybridization of the amplified products to arrays of immobilized primers, (c) single base extension of the immobilized primers (see abstract and Figure 1).

Pastinen teaches that the solid-phase primer extension assay is more accurate than hybridization alone, stating, "The genotypes of homozygous and heterozygous genomic DNA samples were unequivocally defined at each analyzed nucleotide position by the highly specific primer extension reaction. In a comparison to hybridization with immobilized allele-specific probes in the same assay format, the power of discrimination between homozygous and heterozygous genotypes was one order of magnitude higher using the minisequencing method. Therefore, single-nucleotide primer extension is a promising principle for future high-throughput mutation detection and genotyping using high density DNA-chip technology (see abstract)."

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to incorporate single base primer extension (mini-sequencing) as taught by Pastinen into the array hybridization step taught by either of Schubert or Dean. Pastinen expressly taught by single-base primer extension was a more accurate method of genotyping than array hybridization alone (see abstract cited above). An ordinary practitioner would have been motivated by these teachings of Pastinen to further include a single base extension reaction

following array hybridization in the method taught by Schubert or Dean in order to improve the specificity of the assay, and thereby, the accuracy of the resulting genotyping results. Since the method taught by Pastinen was designed for use with amplified products, an ordinary practitioner would have expected a reasonable level of success in adding a single-base extension step in the methods taught by either Schubert or Dean. The combined teachings of Pastinen and Schubert or Dean result in the method of the instant claims 53 and 54.

10. Claims 64 and 66-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastinen et al. (Genome Research, 2000) in view of Zhang et al. (PNAS, 1992) and further in view of Grothues et al. (Nucleic Acids Research, 1992).

Pastinen teaches a method for high-throughput genotyping on oligonucleotide microarrays (see abstract).

Regarding claim 64, Pastinen teaches a method for detecting typable loci of a genome, comprising:

(a) in vitro transcribing a population of amplified genome fragments, thereby obtaining genomic RNA fragments (page 1038, "Multiplex PCR Amplification", where genomic DNA fragments are produced; page 1039 "Optimization of Allele-specific extension reactions" where in vitro transcription of the multiplex PCR products results in genomic RNA fragments; see also Figure 1 for a schematic)

(b) hybridizing said genomic RNA fragments with a plurality of nucleic acid probes having sequences corresponding to said typable loci, thereby forming a plurality of RNA

fragment-probe hybrids (page 1039 "Optimization of allele-specific extension reactions and Figure 1)

(c) detecting typable loci of said RNA fragment-probe hybrids (Figure 1).

Regarding claim 66, Pastinen teaches that step (c) comprises modifying said genomic RNA fragment-probe hybrids with reverse transcriptase (page 1039 "Optimization of allele-specific extension reactions and Figure 1).

Regarding claim 71, Pastinen teaches that modifying the genomic RNA fragment-probe hybrids with reverse transcriptase occurs under conditions wherein DNA-dependent DNA synthesis is inhibited (Figure 1 and page 1039 where the absence of a DNA polymerase inhibits DNA-dependent DNA synthesis).

Regarding claim 72, Pastinen teaches that the method of claim 64 further comprises a step of isolating said genomic RNA fragments (Figure 1 and page 1039 where hybridization of the RNA fragments to specific array-immobilized targets results in their isolation).

Pastinen does not teach the use of random primers comprising a constant region in the in vitro transcription reaction, nor does Pastinen teach replication of the hybridized RNA fragments using locus-specific primers comprising a second constant region followed by an additional replication step using primers complementary to the first and second constant region.

Zhang teaches a method of primer extension preamplification using random primers, as discussed above.

Grothues teaches a method of amplification using tagged random primers.

Regarding claim 64, Zhang and Grothues teach amplification of genomic DNA with random primers (abstract in Zhang and page 1321, column 1 in Grothues)

Regarding claim 67, Zhang teaches amplification of PEP products using a plurality of locus-specific primers (page 5847, column 2), but does not teach that the fragments are RNA.

Regarding claim 68, Grothues teaches amplification using random primers containing a 3' random region and a 5' constant sequence to produce fragments labeled with a constant sequence (2nd paragraph, column 1, page 1321), but does not teach the use of these primers in an *in vitro* transcription reaction.

Regarding claim 69, Zhang teaches the use of locus-specific primers, but does not teach that these locus-specific primers contain an additional constant region.

Regarding claim 70, Grothues teaches further amplification using a primer complementary to the constant tagged region (page 1321, column 1, 2nd paragraph), but does not teach that the first and second constant regions are different.

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize a combination of tagged random and locus-specific primers as taught by Zhang and Grothues in the method of Pastinen in order to improve the accuracy of the hybridization results obtained. Pastinen taught hybridization of *in vitro* transcribed RNA fragments to an array followed by reverse transcriptase mediated allele-specific primer extension (see above). In the method of Pastinen, an amplified population of genomic fragments was produced by multiplex PCR. Regarding claims 64 and 67, an ordinary practitioner of the method taught by Pastinen would have been motivated to incorporate the teachings of Zhang and perform the genomic DNA amplification using random primers in order to eliminate the need for

optimization of a complicated multiplex PCR. Then, following in vitro transcription and hybridization to immobilized probes as taught by Pastinen, an ordinary artisan would have been motivated to perform an amplification step using the locus-specific primers of Zhang in order to provide an additional measure of the accuracy of the hybridization reaction. With regard to claims 68-70, the ordinary user of the method of Pastinen, would have been further motivated by the teachings of Grothues to incorporate constant regions into the random and locus-specific primers, thereby enabling an additional amplification reaction using primers complementary to the constant regions, thus providing another level of control over the accuracy of the hybridization results obtained. Amplification with random primers followed by locus-specific primers was well known in the art, as was the use of tagged primers. Therefore, the ordinary artisan would have readily incorporated the teachings of Zhang and Grothues into the method of Pastinen, in order to effect the improvements discussed above, with a reasonable expectation of success. Therefore, the person of ordinary skill, interested in improving the accuracy of the hybridization data obtained in the method of Pastinen et al., would have been motivated to incorporate tagged random and locus-specific primers as taught by Zhang and Grothues, thus resulting in the instantly claimed methods.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1, 3, 6, 9, 12, 18, 22, 25, 28, 31, 37, 39, 42, 44, 45, 48, 53, 54, and 78-80 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 108, 119-121, 123, and 125-127 of copending Application No. 11/006,096. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 108, 123, and 127 of the '096 application recite a more specific embodiment of the method more generically claimed in the instant claims 1, 6, 18, 25, 78, and 79, and therefore anticipate these claims. Likewise, claims 108, 123, and 125-127 of the '096 application recite a more specific embodiment of the method more generically claimed in the instant claims 37, 42, and 80, and therefore anticipate this claim. The limitations of the instant claims 3, 22, and 39 are recited in claim 108 of the '096 application. The limitations of the instant claims 9, 12, 28, 31, 45, and 48 are recited in claims 119-121 of the '096 application. The limitations of the instant claims 53 and 54 are recited in claim 125 of the '096 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1, 3, 4, 6, 9, 12, 18, 22, 23, 25, 28, 31, 37, 39, 40, 42, 44, 45, 48, 53, and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 78-80, 82, 85, 86, 90, 92, 93, 98, 104-106, 108, 110, 111, 115, 117, 118, and 123 of copending Application No. 10/872,141. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 78, 92, 104, and 117 of the '141 application recite a more specific embodiment of the method more generically claimed in the instant claims 1, 6, 18, and 25, and therefore anticipate these claims. Likewise, claims 78, 85, 92, 98, 104, 110, 117, and 123 of the '141 application recite a more specific embodiment of the method more generically claimed in the instant claims 37 and 42, and therefore anticipate these claims. The limitations of the instant claims 3, 22, and 39 are recited in claims 90 and 115 of the '141 application. The limitations of the instant claims 4, 23, and 40 are recited in claims 93 and 118 of the '141 application. The limitations of the instant claims 9, 12, 28, 31, 45, and 48 are recited in claims 79, 80, 82, 105, 106, and 108 of the '141 application. The limitations of the instant claims 53 and 54 are recited in claim 86 and 111 of the '141 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 1, 3, 4, 6, 9, 12, 18, 22, 23, 25, 28, 31, 37, 39, 40, 42, 44, 45, 48, 53, and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 78, 82-84, 86, 89, 90, 94, 95, 100, and 107 of copending Application No. 10/871,513. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 78, 82, 94, and 107 of the '513 application recite a more

specific embodiment of the method more generically claimed in the instant claims 1, 6, 18, and 25, and therefore anticipate these claims. Likewise, claims 78, 82, 89, 94, 100, and 107 of the '513 application recite a more specific embodiment of the method more generically claimed in the instant claims 37 and 42, and therefore anticipate these claims. The limitations of the instant claims 3, 22, and 39 are recited in claim 78 of the '513 application. The limitations of the instant claims 4, 23, and 40 are recited in claim 95 of the '513 application. The limitations of the instant claims 9, 12, 28, 31, 45, and 48 are recited in claims 79, 82-84, and 86 of the '513 application. The limitations of the instant claims 53 and 54 are recited in claim 90 of the '513 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 1, 3, 4, 6, 9, 12, 18, 22, 23, 25, 28, 31, 37, 39, 40, 42, 44, 45, 48, 53, and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 78, 81, 82, 84, 87, 91, 93, 94, and 104 of copending Application No. 10/870,710. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 78, 91, 93, and 104 of the '710 application recite a more specific embodiment of the method more generically claimed in the instant claims 1, 6, 18, 25, 37, and 42, and therefore anticipate these claims. The limitations of the instant claims 3, 22, and 39 are recited in claim 91 of the '710 application. The limitations of the instant claims 4, 23, and 40 are recited in claim 94 of the '710 application. The limitations of the instant claims 9, 12, 28, 31, 45, and 48 are recited in claims 79, 81, 82, and 84 of the '710 application. The limitations of the instant claims 53 and 54 are recited in claim 87 of the '710 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

16. Claim Objections

Applicant's arguments, see page 11, filed June 16, 2006, with respect to the objection to claim 34 have been fully considered and are persuasive. The objection to claim 34 has been withdrawn.

Rejections under 35 U.S.C. 112, 2nd paragraph

Applicant's arguments, see page 12, filed June 16, 2006, with respect to the rejection of claims 13 and 19 have been fully considered and are persuasive. Applicant's amendment to the claims correcting the antecedent basis problems overcomes the rejections, and therefore, they have been withdrawn.

Rejections under 35 U.S.C. 102

A. Zhang

Applicant's arguments, see page 12, filed June 16, 2006, with respect to the rejection of claims 1-7, 11, 14, 15, 17-20, 22-26, 30, 34, 34 and 36 as anticipated under 102(b) by Zhang have been fully considered and are persuasive. Zhang does not teach all of the elements of the amended claims 1 and 18, and therefore the rejection has been withdrawn.

B. Wigler

Applicant's arguments, see pages 12-13, filed June 16, 2006, with respect to the rejection of claims 1-3, 7-12, 14, 15, 17, 18, 20-22, 26-31, 33, 34, 36-39, 42-48, 50, 51, 53, 54, 64, 66, and 72 as anticipated under 102(e) by Wigler have been fully considered and are persuasive. Wigler does not teach all of the elements of the amended claims 1, 18, 37, and 64, and therefore the rejection has been withdrawn.

C. Dean

Applicant's arguments, see page 13, filed June 16, 2006, with respect to the rejection of claims 1-3, 6, 7, 11, 15, 17-20, 22, 25, 26, 30, 33, 34, and 36 as anticipated under 102(b) by Dean have been fully considered and are persuasive. Dean does not teach all of the elements of the amended claims 1 and 18, and therefore the rejection has been withdrawn.

D. Pastinen

Applicant's arguments, see page 13, filed June 16, 2006, with respect to the rejection of claims 64, 66, 71, and 72 as anticipated under 102(b) by Pastinen have been fully considered and are persuasive. Pastinen does not teach all of the elements of the amended claim 64, and therefore the rejection has been withdrawn

Rejections under 35 U.S.C. 103

Applicant's arguments with respect to claims 13, 32, 40, 41, and 49 have been considered but are moot in view of the new ground(s) of rejection.

Regarding claims 65 and 67-70, Applicant's arguments are moot in view of the new grounds of rejection presented above. However, Applicant does present arguments that are still relevant to the new rejection. Specifically, Applicant argues that there is no motivation to combine the above references (see pages 16-20 of the response).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, the cited references do provide suggestion/motivation for their combination. As noted above, the teachings of Zhang and Grothues provide motivation for one of ordinary skill to amplify genomic DNA using tagged random primers for use in the method taught by Pastinen in order to avoid the need to optimize a complicated multiplex PCR protocol and also to improve the accuracy of the method. Applicant argues that one of ordinary skill would not be motivated to substitute the multi-step protocol necessitated by incorporation of the teachings of Zhang and Grothues for the single-step protocol taught by Pastinen. This argument was not found persuasive, because an ordinary practitioner of the method taught by Pastinen, directed to high-throughput screening of a large number of mutations, would have been motivated to improve the accuracy of the method in spite of the decreased efficiency. In other words, one of ordinary skill would have recognized that results obtained quickly and inaccurately were of less

value than results obtained slightly more slowly, but more accurately. Applicant also argues that one of ordinary skill would not have been motivated to perform whole genome amplification as suggested by Grothues and Zhang, because the complexity of the resulting products could not easily be screened using the array-based methods taught by Pastinen. This argument was also not found persuasive, because oligonucleotide arrays containing probes specific to thousands of genes were readily available at the time of the Pastinen reference (see, for example, Lipshutz et al., cited above). Since Pastinen taught that the mini-sequencing method was primarily limited by multiplex PCR capabilities (page 1033), an ordinary practitioner would have recognized that the whole genome amplification methods taught by Zhang and Grothues offered an alternative means of generating a large number of different amplified products for array analysis. Moreover, since Pastinen taught that higher degrees of multiplexing (i.e. higher sample complexity) would be possible without a loss of discrimination power (page 1037), an ordinary practitioner would have been especially motivated to utilize whole genome amplification as taught by Zhang and Grothues as a means of more easily generating a complex sample for use in the high-throughput genotyping method taught by Pastinen with a reasonable expectation of success.

Double patenting rejections

Applicant requests that the issue of double patenting be held in abeyance until allowable subject matter is indicated in the present application (see page 20 of the response). This request is noted, and the rejections (modified as necessary to account for claim amendments) are reiterated above.

Conclusion

No claims are currently allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Mir (US 2004/0248144 A1), Ji (US 2003/0108870 A1), and Kurn (US 2005/0019793 A1) teach whole genome amplification followed by array hybridization.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is 571-272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Angela Bertagna
Examiner, Art Unit 1637
November 21, 2006
amb

JEFFREY FREDMAN
PRIMARY EXAMINER
11/22/06